



AUSTRALIS
PHARMACEUTICALS

Corporate Presentation

July, 2025

- Australis Pharmaceuticals (Australis) was founded to develop naturally derived compounds into **cancer therapeutics**
- The original compounds were discovered in honey bee propolis on Kangaroo Island in South Australia and characterized as **microtubule-destabilizing agents (MTAs)**
- **AUS_001, oncology lead compound**, has demonstrated encouraging in-vitro and in-vivo data in efficacy and toxicity studies across multiple tumor lines
- Given the broad anti-cancer activity against solid tumors demonstrated by AUS_001 and the ability to cross the **blood brain barrier**, the Phase 1 study will have a broad inclusion criteria for tumor types
- **Orphan Drug Designation** issued for AUS_001 for **malignant gliomas** in February, 2025 and **Rare Pediatric Disease Designation** issued for AUS_001 for **pediatric high grade gliomas** in March, 2025
- Team in place has strong research and clinical development expertise

	Pancreatic Cancer ¹	Malignant Glioma²	Pediatric-type Glioma³
US Incidence	66,440	22,654	~8,800
Estimated Survival	12.8% (5 year survival)	~10% (5 year survival)	Most patients do not survive more than 1 – 2 years

No therapies currently in clinical trials identified as having viable potential to address these great unmet needs for patient

*: these represent just a few of the potential tumor types that AUS_001 can target

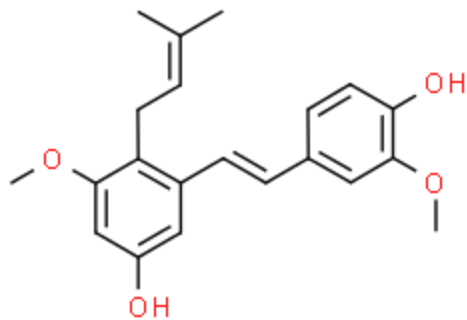
¹ National Cancer Institute SEER database; ² Mesfin, et al. 2024; Ostrom et al., 2022 ³ Gajjar et al., 2022

*AUS_001 extracted from the sedge plant
(source of Kangaroo Island propolis)*

AUS_001 Structure

(E-stilbene)

MW=340.42 g/mol



Common name:

(3-[(E)-2-(4-Hydroxy-3-methoxyphenyl)vinyl]-5-methoxy-4-(3-methyl-2-buten-1-yl)phenol

MECHANISM OF ACTION (MOA)*:
AUS_001 is characterized as a microtubule-destabilizing agent and has demonstrated cell cycle inhibition and induction of programmed cell death. Reversible mode of target engagement and increased uptake by cancer vs. normal cells

Efficacy

- **Pre-clinical efficacy:** Demonstrated across a range of tumor types, including **glioma and other tumor types representing unmet needs for patients**
- **Crosses the blood brain barrier**

Safety

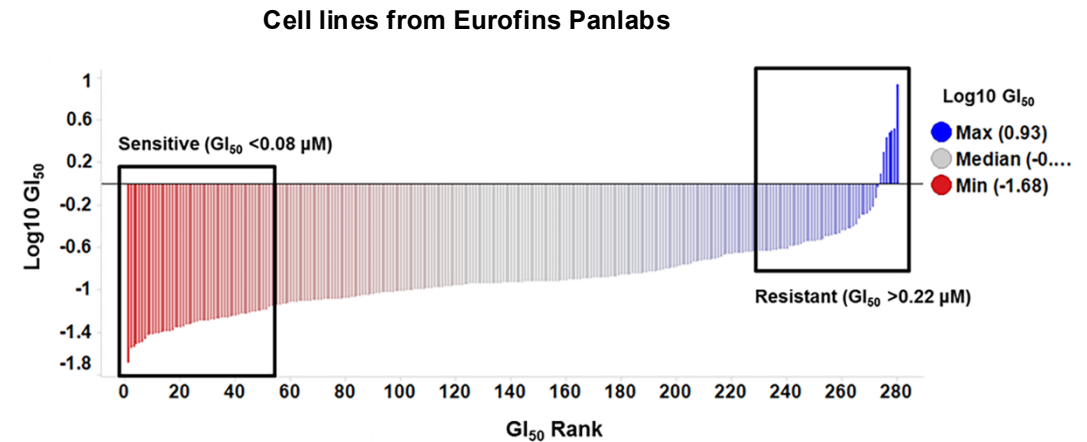
- **Safety margin:** 20-40x more of AUS_001 needed to inhibit growth of healthy non-neoplastic counterpart cells
- **Peripheral neuropathy:** Reversible neurotoxic effect
- **Drug-Drug interactions:** Poor inhibitor of CYP enzymes, common pathway for drug metabolism

Patient Focus

- **Developing an oral formulation**
- **Potential balance of efficacy and safety,** based on pre-clinical therapeutic index

In Vitro Data

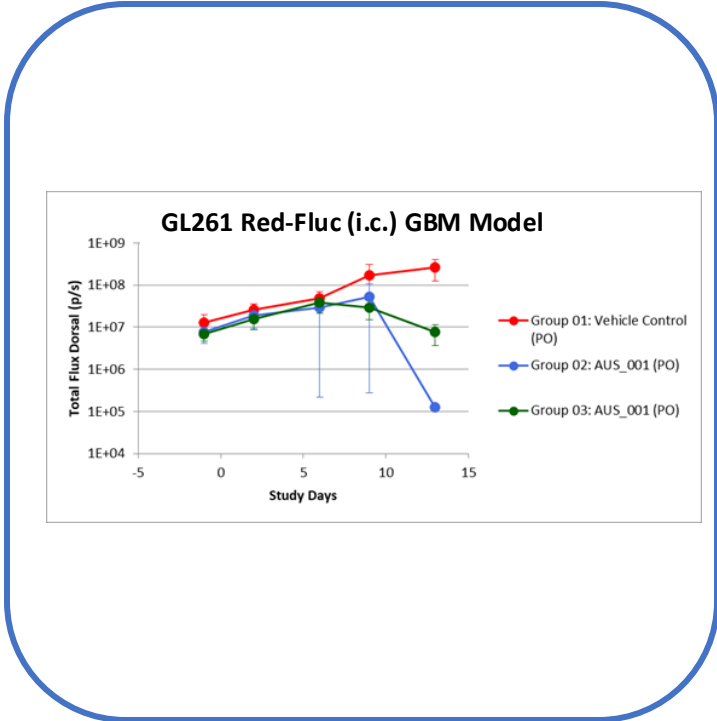
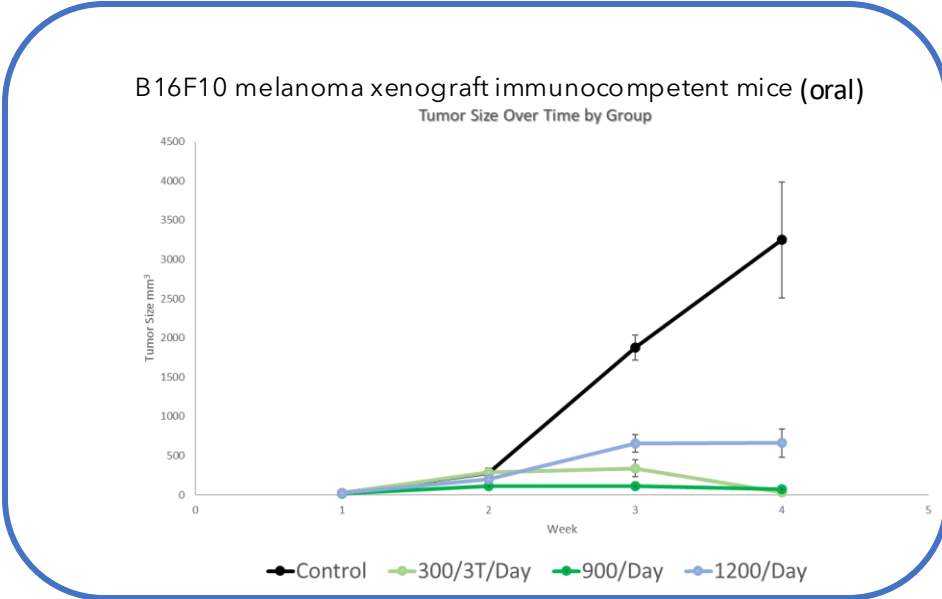
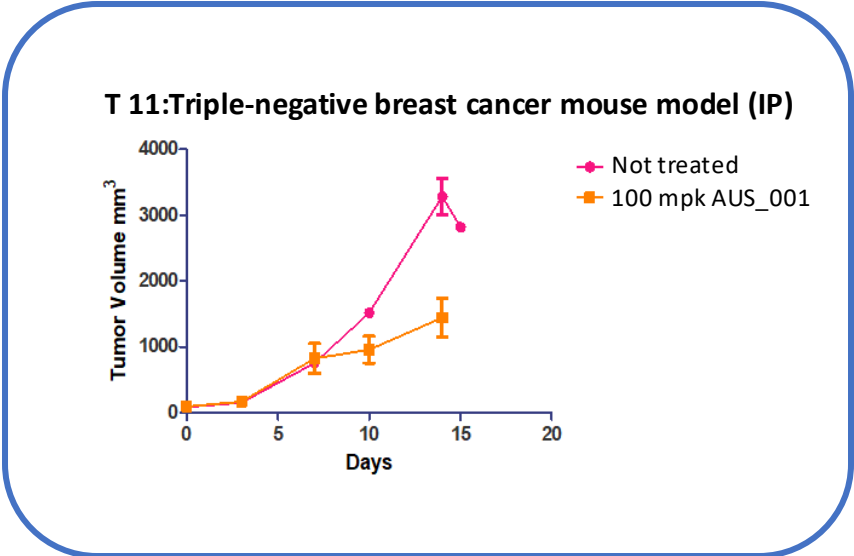
- High potency against **24 types of cancer***, including glioblastoma and other tumor types representing unmet needs for patients
- Encouraging safety margin: **20-40x** more of AUS_001 needed to inhibit growth of healthy non-neoplastic counterpart cells
- Reduced concern for **peripheral neuropathy**: Drug treated midbrain and cortical neurons showed reversible neurotoxic effect for AUS_001 but Paclitaxel-treated neurons suffered sustained neurotoxicity even after discontinuation of treatment
- Less susceptibility to **Drug Resistance-related mechanisms**



The proliferation response of 280 cancer cell lines to AUS_001 treatments as assessed by high-content fluorescence imaging (Eurofins Panlabs): All cell lines with cell count GI₅₀ < 0.08 µM were classified as sensitive to AUS_001, while those with GI₅₀ > 0.22 µM were classified as resistant.

In Vivo Data

- Efficacy established in 7 different in vivo cancer models*
- Crossing of blood-brain barrier**
- Pharmacokinetics/Pharmacodynamics: Accumulation in tumors, organs and brain tissues
- Lack of myelosuppression or other overt toxicities in immunocompetent mouse study (21 days, P.O.)
- Non-emetic response in ferrets



*: Figures to the right depict a few in vivo models; Additional data available upon request

** : Assessed using the 3D Human Blood Brain Barrier Model

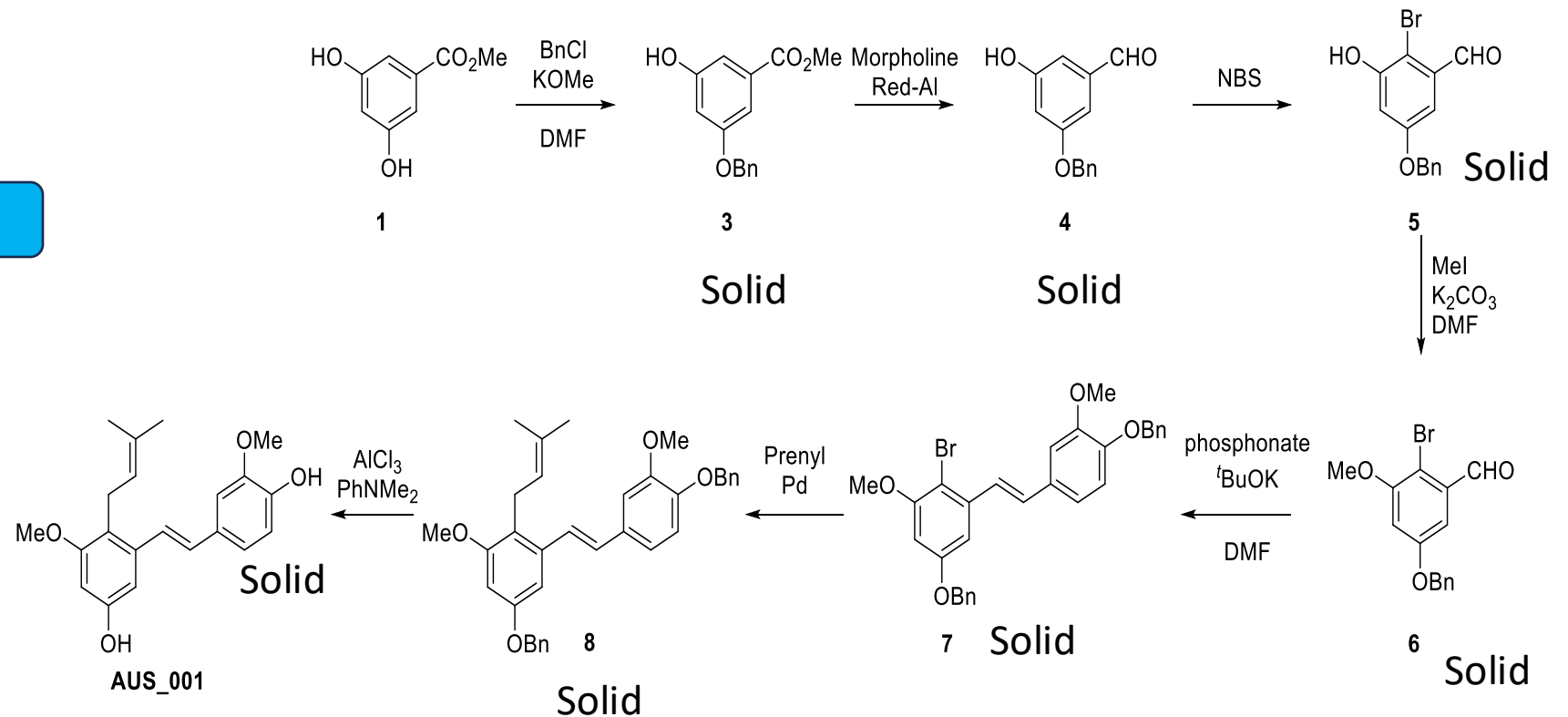
Toxicology Study	Results
AMES Test	No mutagenic potential up to 100 μ M doses of AUS_001
Liver	Poor inhibitor of CYP enzymes, except for CYP1A
Cardiovascular	Low hERG-blocking liability with a half-maximal inhibitory concentration of 65 μ M
P-glycoprotein (P-gp) model	P-gp overexpressing cellular models do not confer resistance to AUS_001
Vascular	AUS_001 affects activated Human Umbilical Vein Endothelial Cells (HUVECs) at lower doses relative to those required for cytotoxicity induction of quiescent endothelial cells

The results of these studies are all encouraging and have a low level of concern for potential patient impact

Synthesis and Manufacturing

- 9 step synthesis of drug substance established -- see figure below
- Currently developing scalable manufacturing (no chromatography)

Synthesis Process



AACR 2024

AACR 2024

ASCO 2024

SITC 2024

ASCO GI 2025

The novel microtubule-destabilizing compound AUS_001 maintains unique binding to the colchicine site of tubulin and elicits reversible cellular effects relative to other anti-tubulin agents

Abstract No: 7141 Herman Lelie¹, Yao-Chieh Chou², Alastair J. King², Zlata Boiarska³, Andrea E. Prota⁴, Michel O. Steinmetz², Marina Koutsoumpa¹

A novel microtubule disruptor exerts broad anticancer efficacy with a tolerable safety profile

Herman Lelie¹, Inger Brandsma², Giel Hendriks², Lee R. Cavedine³, Brogan A. Epkins³, Steven M. Garner³, Andrew J. Cook³, Muthukrishnan Renganatha

The microtubule-destabilizing agent AUS_001 is an attractive candidate for glioblastoma therapy

Abstract No: 3114 Marina Koutsoumpa¹, Aaron L. Carlson², Teresa M. DesRochers², Peter Y.W. Chan³, April L. Risinger³, Robert Adams⁴, Cedric Bardy⁴, Daniel Thomas⁵, Herman Lelie¹

The microtubule-destabilizing agent AUS_001 acts as an immunogenic cell death inhibitor

Abstract No: 976 Marina Koutsoumpa¹, Herman Lelie¹

Implication of the novel microtubule targeting agent, AUS_001, in pancreatic cancer cellular signaling

Abstract No: 748 Marina Koutsoumpa¹, Herman Lelie¹, Kun-Yuan Lin², Pony Yu-Ling Lee²

Our previous work showed that proliferative responses, as assessed using Real Time Tubulin (RTT) C, presented as percent inhibition of a non-linear, least squares regression calculated using the equation of coefficient (n), defining the slope

1. AUS_001

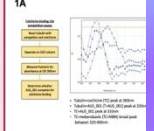


Figure 1. (A) Direct absorbance reaction curves passed over 62 evaluated in Real Time Tubulin (RTT) C presented as percent inhibition of a non-linear, least squares regression calculated using the equation of coefficient (n), defining the slope

3. AUS_001 is

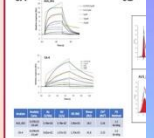


Figure 3. (A) Surface Plasmon Resonance (SPR) analysis of AUS_001 binding to tubulin. Plots were with flow cytometry was performed targeting agents (MTAs) at 10μM for 10 min. CellTiter-Glo

1. AUS_001 exerts broad in vitro anti-cancer activity



Figure 1. The proliferation response of cancer cell lines to AUS_001 was assessed by high-content fluorescence imaging (Eurofins Panlabs). (A) lines with cell count G150 <0.08 μM were classified as sensitive to AUS_001 while those with G150 >0.22 μM were classified as resistant. (B) Dose-response curves for 50% of maximal inhibition of cell growth (G150) on cell lines of the 19 most sensitive cancer types (site of primary tumor breakdown of cell lines classified as sensitive, resistant, or intermediate each cancer type represented in the OncoPanel™ Profiling Analysis. PI are relative to the total number of cell lines for each tissue/tumor type.

2. Orally administered AUS_001 is well-tolerated in vivo

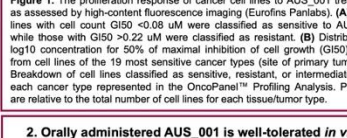


Figure 2. (A) BALB/c mice were treated once daily with 3 different AUS_001 doses (600, 800, 1000 mg/kg). Mice tolerated up to 1000 mg/kg of AUS_001 without significant changes in clinical outlook or weight for at least 14 days. BALB/c nude mice were treated every 3 days with 3 different AUS_001 doses (100, 200 mg/kg). AUS_001 presented significant tumor growth delay in all

1. AUS_001 crosses the Blood Brain Barrier

Microtubules are a well-established target for cancer treatment and decreased toxicity and the ability to also retain efficacy in a subset of 15 established glioma cell lines with

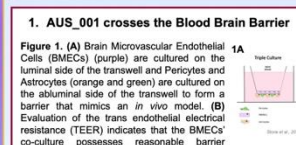


Figure 1. (A) Brain Microvascular Endothelial Cells (BMECs) (purple) are cultured on the luminal side of the transwell and Pericytes and Astrocytes (orange and green) are cultured on the abuminal side of the transwell to form a barrier that mimics an in vivo model. (B) Evaluation of the trans endothelial electrical resistance (TEER) indicates that the BMECs co-culture possesses reasonable barrier tightness (TEER >15040 Ohm*cm²) on Day 6 upon system activation. BMECs treated with 10μM AUS_001 for 6h exhibited strikingly decreased TEER across 2 independent biological replicates. Drug passage through the membrane was confirmed using LC-MS and the apparent permeability coefficient (Papp) was calculated based on the permeation rate and compound concentration.

4. βIII-tubulin overexpression confers limited resistance to AUS_001

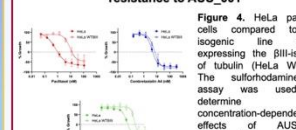


Figure 4. HeLa cells compared to isogenic line st expressing the βIII-iso of tubulin (HeLa WT) The sulfhodamine assay was used to determine concentration-dependent effects of AUS_001. Paclitaxel and Combestatatin A-4 on proliferation of cancer cells over a 48h period. concentration that inhibit cellular proliferation by 50% (G150) was calculated.

1. AUS_001 induces the release of high mobility group box 1 protein and extracellular adenosine triphosphate in a manner from dying cancer cells

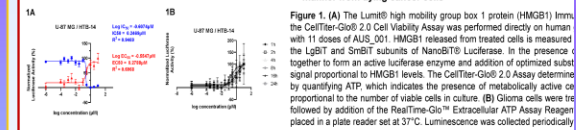


Figure 1. (A) The Lumifluo high mobility group box 1 protein (HMGB1) Immunoassay (Lumifluo HMGB1) was performed directly on human MIA PaCa-2 cells with 11 doses of AUS_001. HMGB1 released from treated cells is measured by the Lumifluo HMGB1 assay. (B) Extracellular ATP release was measured by the Lumifluo ATP assay. (C) Extracellular ATP release was measured by the Lumifluo ATP assay. (D) Extracellular ATP release was measured by the Lumifluo ATP assay. (E) Extracellular ATP release was measured by the Lumifluo ATP assay.

3. AUS_001 stimulates the secretion of essential chemotactic factors for immune effectors

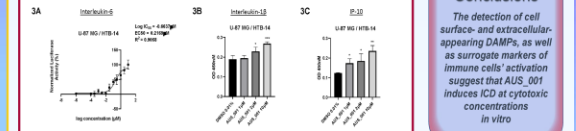


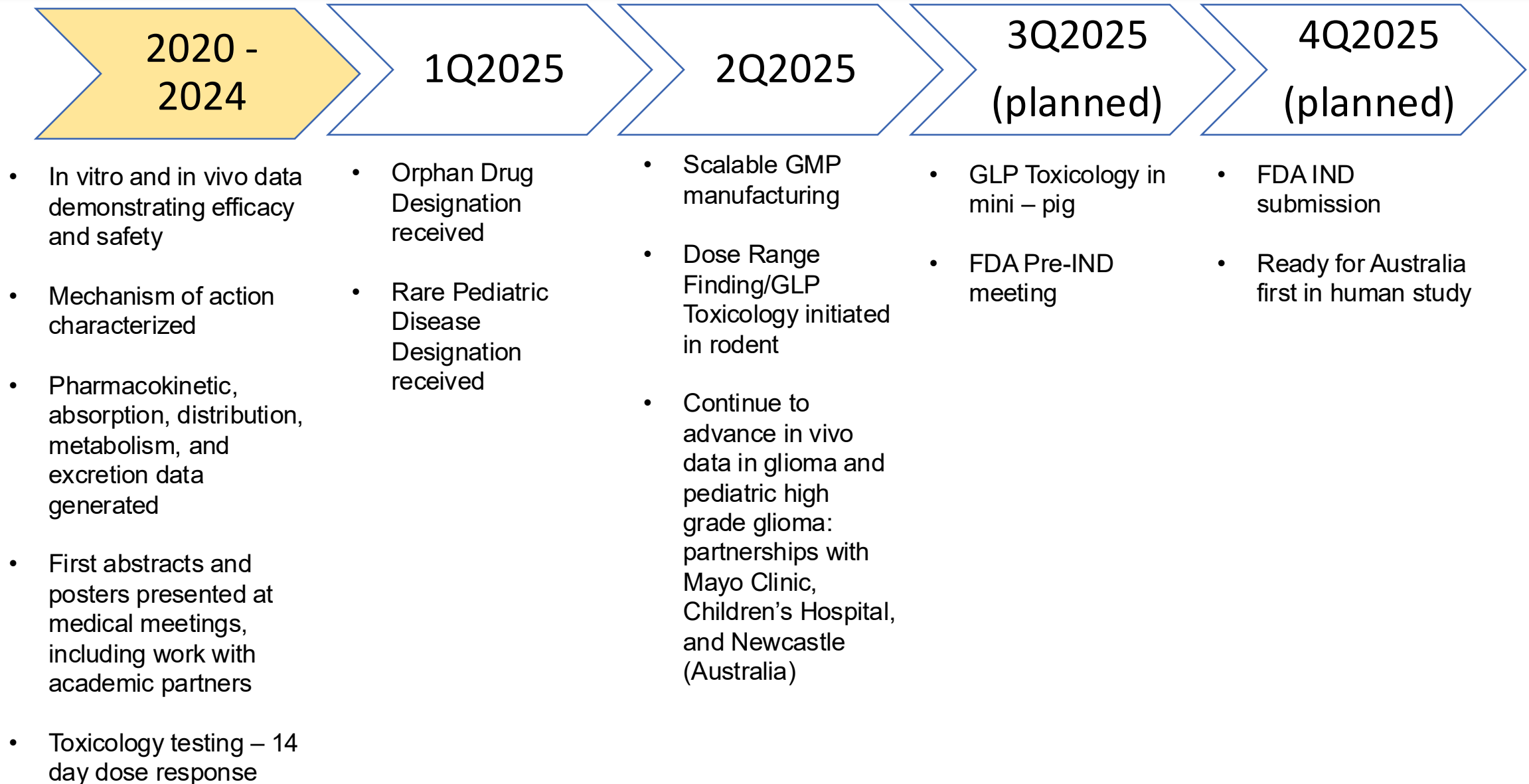
Figure 3. Quantitative measurements of AUS_001-induced release of cytokines were employed using the (A) Lumifluo Interleukin-1β (Human) Immunoassay (Promega) or targeted enzyme-linked immunosorbent assays for (B) Interleukin-3 and (C) C-X-C Motif Chemokine Ligand 10 (IP-10) upon 48h treatment.

Conclusions
The detection of cell surface- and extracellular- appearing DAMPs, as well as surrogate markers of immune cells' activation suggest that AUS_001 induces ICD at cytotoxic concentrations in vitro

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Conclusions
Our findings provide critical insights into the molecular events triggered by AUS_001 in PanCa cells and serve as a valuable resource for future exploration of AUS_001 as a novel PanCa therapeutic agent

Global Patents/Exclusivity	Expiry
2012: Use and synthesis of AUS_001 and one pipeline asset	2032
2020: Covers 4 pipeline assets, new synthesis route and 5000+ potential new chemical entities	2040
Orphan Drug and Rare Pediatric Designations	~ 7 year extension following approval



Australis Pharmaceuticals Executive Team

Team Member	Role	Expertise	Past Experiences
Todd Robinson	Founder	Entrepreneur with business and financial expertise. Owner of the land where AUS_001 was discovered	Building and leading organizations across many industries
Michele Korfin, RPh, MBA	CEO	~30 years as a Biotech leader	Merck, Celgene, Kite, TYME, Gamida Cell
Caroline Carr, CPA	CFO	Finance leader in Biotech and Pharma companies	Mycovia, Dara, Pfizer, Deloitte
Marina Koutsioumpa, PhD	VP, Cancer Biology	PhD with expertise in cancer biology and molecular pharmacology	UCLA Center for Systems Biomedicine
Herman Lelie, PhD	VP, Research and Development	PhD with expertise in analytical chemistry and pre-clinical development	MIT, UCLA, Bruin Biometrics, Constitution Labs

Australis Pharmaceuticals Funding

Successfully raised ~\$30M over the last 10+ years

No debt on the balance sheet

Enough cash on hand to proceed through Phase 1

- AUS_001 has demonstrated encouraging pre-clinical efficacy with a large safety margin
- Completing IND enabling studies this year and will plan to be ready for first in human studies by the end of 2025
- Experienced scientific team who have partnered very effectively with academic institutions
- Leadership team with expertise in advancing oncology therapies through FDA approval and launch
- Business goals for 2025:
 - Biotech/pharmaceutical partnerships to advance our clinical research
 - Continue to enhance our balance sheet for our clinical trial work beyond first in human